Nicorandil: mucocutaneous ulceration (continued)

- A very severe case report.

In 2012, a summary of an exemplary case report of adverse effects attributed to nicorandil was published in the newsletter of the Regional Pharmacovigilance Centre in Angers, France (1). Nicorandil has low efficacy as a symptomatic treatment for angina pectoris. It is known to cause sometimes severe ulceration of the skin and mucosae (2).

An 87-year-old woman who had been taking nicorandil since 2003 developed severe aphthous stomatitis in mid-2009 (1). Nicorandil was discontinued in July 2009 and the lesions healed within a month. In August, nicorandil was reintroduced.

In December 2009, a sigmoidouterine fistula was diagnosed. In March 2011, a colostomy was performed. Then, a vesicouterine fistula was diagnosed. In December 2011, a sigmoidouterine fistula was diagnosed. In March 2011, a vesicouterine fistula was diagnosed. The stoma area became ulcerated in August 2011. Nicorandil was withdrawn in August 2011. By late September 2011, the ulceration around the stoma had improved and the pain had stopped. By November 2011, it had almost completely healed.

In view of nicorandil's minor efficacy in angina, these adverse effects are unacceptable: patients would be better served if nicorandil were neither prescribed, used nor licensed.

Selected references from Prescrire’s literature search.

Varenicline and bupropion: suicide

- An analysis of reports in the USA.

In late 2011 a study based on reports made between 1998 and 2010 to the US Food and Drug Administration (FDA) analysed reactions in patients taking drugs used for smoking cessation, namely varenicline, bupropion and nicotine (1). It included 3249 cases of suicide, self-harm and severe depression, 90% involving varenicline, 7% bupropion, and 3% nicotine.

The authors calculated what proportion these adverse effects represented among all other serious adverse effects reported with each drug.

Compared to nicotine, this proportion was 8 times higher with varenicline (odds ratio 8.4, 95% confidence interval (95%CI): 6.8 to 10.4) and about 3 times higher with bupropion (95%CI:2.3 to 3.7).

The increase persisted after excluding reports in which the patient was also taking one or more of the other 58 drugs for which, according to the US summaries of product characteristics, suicide is an adverse effect.

In practice, varenicline and bupropion both have an unfavourable harm-benefit balance. When a smoker needs a drug to help him or her quit, it is best to use nicotine (2).

Benfluorex: lesions on a bioprosthetic heart valve too

- A troubling case.

In early 2012, a French team published a troubling case report involving a 40-year-old woman who underwent heart valve replacement surgery twice while taking benfluorex (formerly marketed under the brand name Mediator® among other names) (1,2).

After 15 months of benfluorex therapy, the patient was diagnosed with mitral valve regurgitation, and a bioprosthetic valve was implanted.

Benfluorex was reintroduced, and the patient continued treatment for 33 months. Cardiac problems developed a second time. She was diagnosed with mitral and aortic regurgitation, and both valves were replaced with mechanical valves. The lesions on the bioprosthetic mitral valve resembled those on the native aortic valve, including thickening similar to lesions attributed to benfluorex or observed in patients with carcinoid tumours. No other possible causes of valvar heart disease were identified, such as the use of other amphetamine appetite suppressants or ergot derivatives.

Benfluorex therefore also appears to provoke serious valvar injury, even to porcine bioprosthetic valves.

In cases of valvar insufficiency, even those involving a bioprosthetic valve, benfluorex should be systematically suspected as the causative agent, along with other drugs known to damage heart valves.

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